Clinical review

Acute cholecystitis

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Patients with suspected acute cholecystitis should be referred to hospital and, if the diagnosis is confirmed, early surgery is indicated

Acute cholecystitis—inflammation of the gall bladder—is most often caused by gall stones. Gall stones are one of the most common disorders of the gastrointestinal tract, affecting about 10% of people in Western society.[1] [2] More than 80% of people with gall stones are asymptomatic. Acute cholecystitis develops in 1-3% of patients with symptomatic gall stones.[3]

Helminthic infection (ascariasis) is a major cause of biliary disease in developing countries in Asia, southern Africa, and Latin America.[4] Obstruction of the cystic duct causes an inflammatory process to start. This results in acute cholecystitis. If the inflammation persists it may cause perforation or gangrene of the gall bladder.

Diagnosis of acute cholecystitis is made on the basis of clinical features and is supported by results of ultrasound scanning. Treatment is predominantly surgical, although the timing of surgery is under debate.

Methods

We prepared this review by searching Medline for articles in English that included the term "acute cholecystitis." We looked at clinical trials with clear end points and conclusions, and present findings of trials that reflect most of the work published.

Pathogenesis

Over 90% of cases of acute cholecystitis result from obstruction of the cystic duct by gall stones or by biliary sludge that has become impacted at the neck of the gall
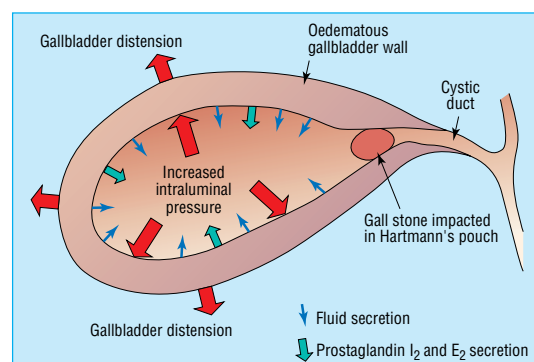

Fig 1 Pathogenesis of acute cholecystitis

Summary points

Acute cholecystitis is most often caused by gall stones

Patients suspected of having acute cholecystitis should be referred to hospital immediately

First line treatments include fasting, intravenous fluids, and analgesia

Surgery (cholecystectomy) within 24-48 hours of admission (early) is preferable to delayed or "interval" surgery

Percutaneous cholecystostomy is a safe alternative to cholecystectomy for very ill patients or those unfit to undergo surgery

In 20% of cases, emergency surgery is needed to treat gangrenous cholecystitis or gallbladder perforation

bladder. Obstruction of the cystic duct causes the intraluminal pressure within the gall bladder to increase and, together with cholesterol supersaturated bile, triggers an acute inflammatory response. The trauma caused by the gall stones stimulates the synthesis of prostaglandins I_2 and E_2, which mediate the inflammatory response (fig 1).[5] Secondary bacterial infection with enteric organisms (most commonly *Escherichia coli*, *Klebsiella*, and *Streptococcus faecalis*) occur in about 20% of cases.

Biliary sludge is a mixture of particulate matter and bile, and it may stimulate microlithiasis. If the sludge persists—for example, because the patient has already had several pregnancies or is receiving total parenteral nutrition—gall stones can form.[6] Most patients with biliary sludge have no symptoms, but the sludge itself can cause acute cholecystitis.

Presentation and diagnosis

Acute cholecystitis is diagnosed on the basis of symptoms and signs of inflammation in patients with peritonitis localised to the right upper quadrant (fig 2).

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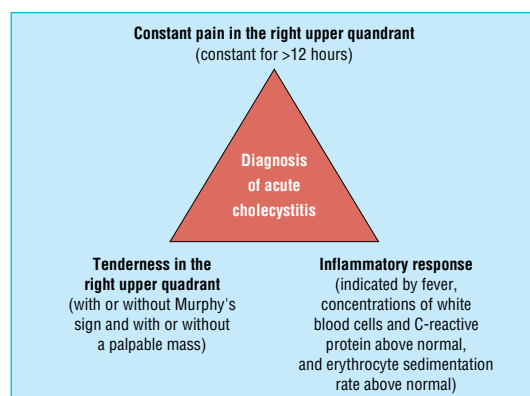
Fig 2 Clinical features of acute cholecystitis: diagnosis is made when features from all three points of diagnostic triangle are present

Acute cholecystitis should be differentiated from biliary colic by the constant pain in the right upper quadrant and Murphy's sign (in which inspiration is inhibited by pain on palpation). Patients with acute cholecystitis may have a history of attacks of biliary colic or they may have been asymptomatic until the presenting episode.

In patients with superimposed bacterial infection, septicaemia develops and is associated with increased morbidity and mortality. Patients with severe acute cholecystitis may have mild jaundice (serum concentrations of bilirubin < 60 µmol/l) caused by inflammation and oedema around the biliary tract and direct pressure on the biliary tract from the distended gall bladder. Concentrations of bilirubin > 60 µmol/l suggest a diagnosis of choledocholithiasis (a gall stone in the common bile duct) or Mirrizzi's syndrome (obstruction by a stone impacted in Hartmann's pouch that compresses the common hepatic duct). All patients suspected of having acute cholecystitis should be referred to hospital.

Investigations

Ultrasound scanning is the investigation of choice in patients suspected of having acute cholecystitis. Sonograms typically show pericholecystic fluid (fluid around the gall bladder), distended gall bladder, oedematous gallbladder wall, and gall stones, and Murphy's sign can be elicited on ultrasound examination (fig 3). Colour flow Doppler ultrasound shows hyperaemic, pericholecystic blood flow and acute inflammation.[7] Plain abdominal radiographs show radio-opaque gall stones in about 10% of cases of acute cholecystitis and gas within the gallbladder wall in emphysematous cholecystitis (fig 4).

Biliary scintigraphy (hydroxyiminodiacetic acid (HIDA) scan) is the gold standard investigation when the diagnosis remains in doubt after ultrasound scanning. The patient is given an intravenous injection of radiolabelled hydroxyiminodiacetic acid and then the abdomen is scanned; in patients with acute cholecystitis, the gallbladder lumen will not take up any radioactive isotope one to two hours after injection and therefore the gall bladder will not be visible on the scan. Occasionally, an acutely inflamed gall bladder may have delayed filling, leading to a false positive result, but augmentation with morphine reduces this.[8]

Management

Medical management

Most patients with acute cholecystitis respond to conservative, first line management: the gall stone disimpacts and falls back into the gall bladder, which allows the cystic duct to empty. If the gall stone does not disimpact, complications—such as advanced cholecystitis (gangrenous cholecysytitis or empyema of the gall bladder) or perforation—may result.

Immediate measures should be taken to rest the gall bladder; this will subdue the inflammatory process in most patients. Patients should be fasted, rehydrated with intravenous fluids, and given oxygen therapy and adequate analgesia. Indometacin (25 mg three times daily for a week) can reverse the inflammation of the gall bladder and the contractile dysfunction seen in the early stages (first 24 hours) of cholecystitis. The prokinetic action of indometacin will also improve postprandial emptying of the gall bladder in patients with gallbladder disease.[10] A single intramuscular dose

Fig 3 Ultrasound (B mode) findings in acute cholecystitis
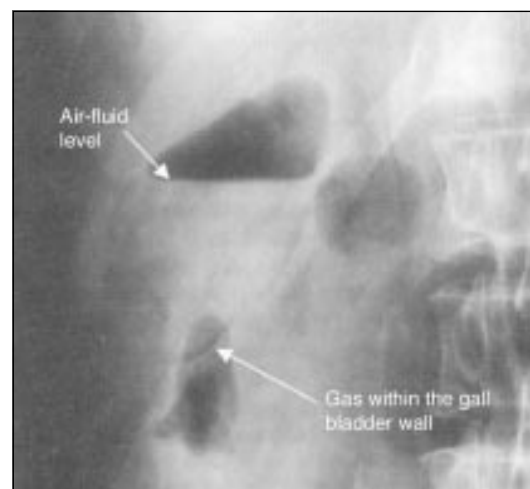
Fig 4 Plain abdominal radiograph showing emphysematous cholecystitis: note gas within the gallbladder wall and air fluid level within the gall bladder

of diclofenac (75 mg) may substantially decrease the rate of progression to acute cholecystitis in patients with symptomatic gall stones.[11] Because of the risk of superimposed infection, intravenous antibiotics should be started empirically if the patient has systemic signs or if no improvement is seen after 12-24 hours. A second generation or newer cephalosporin should be used (for example, cefuroxime 1.5 g every 6-8 hours) with metronidazole (500 mg every 8 hours). Non-operative management—solvent dissolution therapy or extracorporeal shockwave lithotripsy—has been used with variable results to treat chronic cholecystitis in patients unfit for surgery,[12] but it has no place in the management of acute cholecystitis.

Surgical management

About 20% of patients with acute cholecystitis need emergency surgery. Such surgery is indicated if the patient's condition deteriorates or when generalised peritonitis or emphysematous cholecystitis is present. These features suggest gangrene or perforation of the gall bladder.

Cholecystectomy

The timing of surgery for the 80% of patients without evidence of gangrene or perforation is under debate. Open cholecystectomy traditionally has been performed 6-12 weeks after the acute episode to allow the inflammatory process to resolve before the procedure (interval surgery).[13] Patients with acute cholecystitis who undergo early laparoscopic cholecystectomy (before symptoms have lasted 72-96 hours) have lower complication rates and lower conversion rates than open cholecystectomy and shorter hospital stays than those undergoing interval surgery (table). Early surgery for acute cholecystitis also has a lower conversion rate than delayed surgery (which is performed during the index admission after conservative management and after symptoms have lasted 3-5 days) (table).[16 17] Early surgery also avoids complications when conservative treatment fails.[18] A long time between onset of symptoms and presentation is associated with advanced disease (P=0.01).[17]

Early laparoscopic surgery is safe and feasible in patients with acute cholecystitis. If early intervention—less than 72 hours after symptoms started—can be achieved, "oedema planes" present during this period allow the gall bladder to be dissected laparoscopically. Although it is desirable to operate within this time period, it is often difficult to do so in clinical practice. By the time inflammation has been present for more than 72 hours, features of chronic inflammation (such as fibrosis) predominate and make it more difficult to dissect the gall bladder (see box A on bmj.com). The optimal treatment for patients presenting with acute cholecystitis should be resuscitation followed by laparoscopic cholecystectomy on the next available surgical list.

Patients with fever, serum bilirubin >170 μmol/l, male sex, body temperature >38°C, and advanced cholecystitis are more likely to have complications.[17 19]

Percutaneous cholecystostomy

Percutaneous cholecystostomy is a minimally invasive procedure that can benefit patients with serious comorbidity who are at high risk from major surgery. Percutaneous cholecystostomy can be performed at the bedside under local anaesthetic and is suitable for patients in intensive care units and those with burns. It is the definitive treatment in patients with acalculous cholecystitis (see below), or it may be used as a temporising measure—to drain infected bile and delay the need for definitive treatment.

Percutaneous cholecystostomy gives clinical improvement in about three quarters of patients. Mortality after this procedure is related to comorbidity (for example, pneumonia or myocardial infarction) or pre-existing sepsis. An incomplete or poor response to cholecystostomy within the first 48 hours may indicate causes of sepsis other than cholecystitis, inadequate antibiotic coverage, possible complications (such as dislodgement of the drainage tube), or necrosis of the wall of the gall bladder.

Patients can undergo cholecystectomy after percutaneous cholecystostomy. In patients unfit to be given a general anaesthetic, the drain can be left in place for more than six weeks to allow radiological extraction of calculi at a later date.

Conversion rate to open surgery and outcomes after surgery for acute cholecystitis in prospective randomised studies. Values are numbers (percentages) unless otherwise specified

Study	Patients	Procedures converting to open surgery	Outcome		
			Complications	Mean stay in hospital (days)	Mean postoperative stay (days)
Early *v* interval cholecystectomy*					
Lai (1998)[15]	Total (n=104)	22 (22)	NR	NR	NR
	Early surgery (n=53)	11 (21)	5 (9)	7	4
	Interval surgery (n=46)	11 (24)	3 (8)	11	3
Lo (1998)[14]	Total (n=99)	NR	NR	NR	NR
	Early surgery (n=49)	5 (11)	6 (13)	6	NR
	Interval surgery (n=50)	9 (23)	12 (29)	11	NR
Early *v* delayed cholecystectomy*					
Pessaux (2000)[16]	Total (n=132)	51 (39)	NR	NR	NR
	Early surgery (n=85)	23 (27)	12 (14)	7.6	7.9
	Delayed surgery (n=47)	28 (60)	6 (13)	11.4	NR
Eldar (1999)[17]	Total (n=348)	76 (22)	57 (17)	NR	NR
	Early surgery (n=230)	42 (18)	NR	NR	NR
	Interval surgery (n=118)	34 (28)	NR	NR	NR

NR=not reported.
*Early surgery occurs when symptoms have lasted up to 72-96 hours; interval surgery occurs 6-12 weeks after the acute attack; delayed surgery occurs after conservative management during admission for the attack and usually after symptoms have lasted 5 days.

Sequelae of acute cholecystitis

Gangrenous cholecystitis

Gangrenous cholecystitis occurs in 2-30% of cases of acute cholecystitis. Men aged over 50 with a history of cardiovascular disease and leucocytosis ($>17\,000$ leucocytes/ml) have the highest risk of gangrene of the gall bladder.[9] Gangrene occurs most commonly at the fundus because the vascular supply often becomes compromised. Urgent laparoscopic cholecystectomy should be considered in patients at high risk of gangrene, and the surgeon should have a low threshold for conversion to open cholecystectomy during the procedure.

Gallbladder perforation

The gall bladder is perforated in 10% of cases of acute cholecystitis—usually in patients who sought medical attention after a delay or in those who do not respond to conservative management. Perforation most commonly occurs at the fundus. After the gall bladder has perforated, patients may experience transient relief of their symptoms because the gall bladder decompresses, but peritonitis then develops.
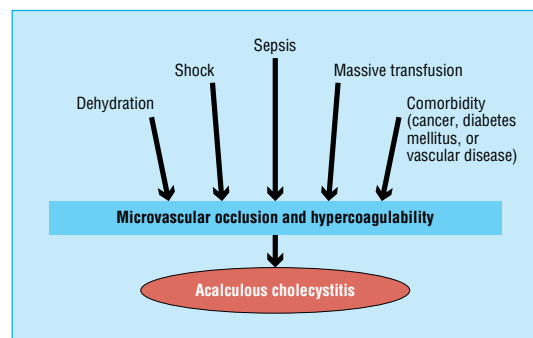
Free perforation presents with generalised biliary peritonitis and is associated with a mortality of 30%. Localised perforation, with the formation of pericholecystic abscesses, is more common, because the adherent viscera adjacent to the perforation tend to localise spillage of the contents of the gall bladder. A mass may be palpable in patients with localised perforation, and computed tomography is the most useful investigation.

Cholecystoenteric fistulas

An acutely inflamed gall bladder may create a cholecystoenteric fistula by adhering to and causing a perforation in other parts of the gastrointestinal tract. The most common sites for fistulas are the duodenum and the hepatic flexure of the colon. Decompression of the gall bladder because of a fistula may cause resolution of the acute cholecystitis. Air in the biliary tree (pneumobilia) can be seen on abdominal radiographs, and imaging enhanced with contrast agents may show fistulas.

Gallstone ileus

Gallstone ileus—obstruction of the small intestine caused by a gall stone passing from the biliary tract into the intestinal tract through a fistula—should be considered in elderly patients with no obvious cause for the intestinal obstruction. Patients may not have a history of cholecystitis. Mortality (15-20%) is attributed

to delays before surgery is performed or to coexisting medical illnesses. Classic findings on abdominal radiographs include pneumobilia, intestinal obstructions, and gall stones in unusual sites.

Acute cholecystitis and pregnancy

Biliary tract disorders are the second most common general surgical condition in pregnancy, with an incidence of symptomatic gallstone disease of $\leqslant 0.1\%$ (acute appendicitis is the most common surgical condition). Surgical intervention should be delayed until after delivery unless conservative treatment fails or symptoms recur in the same trimester. When surgery is indicated in pregnancy, laparoscopic cholecystectomy has been shown to be safe.[20 21]

Acalculous cholecystitis

Acute acalculous cholecystitis is a life threatening condition that occurs in critically ill patients; it accounts for 5-14% of all cases of cholecystitis. The diagnosis is often elusive and is associated with considerable mortality (up to 50%).

Acalculous cholecystitis tends to occur in patients hospitalised for multiple trauma or acute non-biliary illness. Risk factors include severe trauma or burns, major surgery (such as cardiopulmonary bypass), long term fasting, total parenteral nutrition, sepsis, diabetes mellitus, atherosclerotic disease, systemic vasculitis, acute renal failure, and AIDS (fig 5).

Over 70% of patients have atherosclerotic disease; this might explain the high prevalence of the condition in elderly men.[22]

Immunocompromised patients can develop primary infections caused by opportunistic organisms that result in primary infective cholecystitis (see box B on bmj.com).[23 24]

Fig 5 Pathogenesis and risk factors for acute acalculous cholecystitis

The diagnosis of acute acalculous cholecystitis may be hindered by obtundation of the patient, pre-existing disease, or recent abdominal surgery, and it needs a high index of suspicion. Ultrasound scanning is the investigation of choice—it can detect concomitant lesions, it can be performed in intensive care units, and therapeutic interventions (such as percutaneous drainage) can be done simultaneously.

Percutaneous cholecystostomy is an accepted alternative to cholecystectomy in the treatment of acute acalculous cholecystitis.[25] Early cholecystectomy may be appropriate, depending on the patient's clinical condition.

This article is based on a keynote lecture given by IJB to the Association of Upper Gastrointestinal Surgeons at the Royal College of Physicians, Edinburgh, in September 2001.

Competing interests: None declared.

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A patient who changed my life
Two lives saved

As a native Cuban intensive care doctor, I felt many parts of my life were not mine to control. Having free health and education systems does not make you free. Cuban security forces control many aspects of life, as a colleague and I discovered when we tried to publicise some research about the extent of a local epidemic of dengue fever. We were told to stop or face imprisonment because it showed the country in a bad light. This sort of control contrasts with the treatment of visitors to Cuba from old capitalist enemies such as the United States and Britain. Nowhere is this more apparent than in health care. If a foreigner falls ill in Cuba, he or she will be given the best treatments, over and above that which would be given to native Cubans, to show how good communism is.

And so it was that on a particular Sunday lunchtime I was called urgently to the intensive care unit to see a foreigner just admitted with an inferior myocardial infarction. He was an Englishman in his 50s on holiday who had developed chest pain a couple of hours earlier, with no history of heart disease. Of course, if he were Cuban he would have been admitted to coronary care for this, not intensive care. However, almost as soon as I arrived on the unit, and before I had the chance to introduce myself, he collapsed in cardiac arrest. The flurry of resuscitation started immediately. Multiple defibrillations, central line insertion, and endotracheal intubation rapidly followed. This was no easy arrest to manage, as the heart rhythm alternated between ventricular fibrillation and asystole. We kept going, but we were running out of ideas. I was aware of a growing consensus around the bed that we should stop trying. I do not know what made me persist, but I did. Suddenly the electrocardiogram reverted to sinus rhythm and remained so. Miraculously, he made an excellent recovery with no evidence of heart failure or brain damage.

After a few days he was well enough to leave the intensive care unit, by which time I had become friendly with him and his wife. They invited me to visit them in Britain. Disillusioned with Cuba, I decided to take them up on their offer. Who knows what might happen? Finally, after eight months, I was given permission to travel to Britain. When I arrived I was pleased to see that my patient had continued his excellent recovery and was back at work running his pub. During my stay, I was stunned to hear that my colleague in Cuba had been arrested for the "antigovernment propaganda statements" concerning the dengue fever epidemic. I had been thinking about it before I came to Britain, but now the choice was clear: I applied for political asylum.

Five years have passed, and I am happily settled in Britain now. My English patient is grateful to me because he knows how close he was to losing his life. However, I am as just as grateful to him, for helping to save mine. For the first time in my life, I feel truly free and enjoy every new day in this country.

Susana Romero Zambrano *senior house officer, Princess Margaret Hospital, Swindon*